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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1647	13

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/897,438	MIKOSHIBA ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4-14-03* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-8,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-11* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10, 12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

1. The amendment filed 4-14-03 has been entered into the record and has been fully considered.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

3. As a result of Applicant's amendment, all rejections not reiterated herein have been withdrawn by the Examiner.

Rejections Maintained

Election/Restriction

4. Applicant's election of Group II, claims 4-8 and 10-11 in part in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

5. Claims 1-3 and 9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

6. This application contains claims 1-3 and 9 drawn to an invention nonelected with traverse in Paper No. 8. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 4-8 and 10-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO:1, does not reasonably provide enablement for polynucleotides of alternative sequence as claimed including deletion, insertion, substitution and degenerate sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

The skilled artisan readily recognizes that protein chemistry is an unpredictable area of biotechnology. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition, see in particular Skolnick et al., Trends in Biotech., 18(1):34-39, 2000. For example, Jobling et al, Mol. Microbiol., 1991, 5(7):1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which produce proteins that differ in native conformation, immunological recognition, binding and toxicity. Thus, these references exemplify the importance of conserved structural components to both biological function and immunological recognition. The skilled

artisan also recognizes that immunological responses depend upon the structural characteristics (conformation) of the particular protein (amino acid sequence) targeted and that variations in sequence may effect such structure and immunological recognition.

Instant specification discloses a CR-50 epitope designated as SEQ ID NO:2, residues 230-346 of Reelin protein, see in particular p. 4, lines 11-18. However, the claims are drawn generically to polynucleotides encoding a CR-50 epitope region polypeptide of Reelin protein which comprises a CR-50 antibody recognition site but comprises neither a F-spondin domain nor a repeat site, and to polynucleotides encoding a polypeptide comprising SEQ ID NO:2 and deletion substitution or addition mutations of SEQ ID NO:2 as presumably recited in claim 4. The claims are also drawn to polynucleotides of SEQ ID NO:1, to deletion, insertion and substitution mutations as well as to degenerate nucleotide sequences. Thus, the claims are directed to polynucleotides encoding peptides with greater than single amino acid substitutions, deletions and insertions and to partial peptide fragments which bind CR-50 antibody. Yet the specification fails to teach alternative sequences other than SEQ ID NO:2 encoded by SEQ ID NO:1 and degenerate sequences thereof, capable of binding CR-50 antibody that corresponds to the claim recitations. There is no disclosure of those residues which may be replaced, modified, inserted or deleted without abrogating the disclosed immunological reactivity. Moreover, as pertinent in claims 10-11, the specification fails to teach such suitable compositions for stimulating the assembly of Reelin protein molecules or for providing a pharmaceutical for diagnosis or treatment of

diseases resulting from abnormally positioned neurons. At most the specification merely recognizes an eptiope region which binds CR-50 antibody and which spontaneously forms a regular homopolymer via electrostatic interaction as disclosed at p. 4, lines 11-18. Furthermore, Reelin mutants are only recognized in mice and the model system is pertinent only to the Reelin phenotype which does not approximate all recognized abnormally positioned neurons but only those recognized as aberrantly positioned in Reelin animals, see for example Curran et al., Br. Res. & Br. Res. Reviews, 26(2-3):285-94, May 1998.

The specification does not enable the broad scope of the claims that encompass a multitude of analogs or equivalents because the specification does not teach which residues can or should be modified such that the polypeptides retain sufficient structural similarity to evoke immune responses or to provide for the required effects. The specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful and the skilled artisan would not expect functional conservation or immunological recognition among homologous sequences. Thus, applicants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed derivatives in a manner reasonably correlated with the scope of the claims. The artisan recognizes that such structure is critical to antibody binding. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly,

extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

Thus, in view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives and fragments encompassed by the claims, one skilled in the art would be forced into undue experimentation in order to determine those peptides which correlate to the recitations of the claims, i.e., to define those residues capable of CR-50 monoclonal antibody binding, stimulating the assembly of Reelin proteins or diagnosing or treating diseases associated with abnormally positioned neruons. Further the artisan would be required to confirm the peptides utility in the process of making and using a polypeptide capable of stimulating an antibody capable of binding reelin products, thus inhibiting Reelin function, see in particular Utsunomiya-Tate N., et al., PNAS, 97(17):9729-34, Aug. 15, 2000. Therefore, the enablement provided by the specification, in view of the skill in the art, is not commensurate in scope with the claims.

Applicants argue in the amendment of 4-14-03 that the making and testing of peptides modified from SEQ ID NO:2 that bind antibody CR-50 is not undue experimentation in accordance with *In re Wands*. Applicant's further argue with respect to claim 10, that the specification at p. 9, lin2 24-p.10, line 6 provide mechanisms such as Western blot analysis with anti-Reelin antibodies as a mechanism for determining those compositions capable of stimulating the assembly of Reelin molecules. Moreover, with respect to claim 11, applicant's argue that the specification at p. 13, lines 8-18 discuss diseases capable of treatment with the claimed polynucleotides and

peptides. In particular, applicants argue that lissencephaly, polymicrogyria and ectopic gray matter are such diseases capable of treatment and thus that the full scope of the claims are enabled. Applicant's respond to the lack of structure function correlation by amendment requiring CR-50 antibody recognition, relation to SEQ ID NO:2 or a mouse Reelin protein.

Applicant's arguments filed 4-14-03 have been fully considered but are not persuasive to the full scope of the claim. The ability to "make and test" is not the standard for an enabling disclosure. The instant specification fails to identify that structure which is required for the claimed biological activities of, "a CR-50 antibody recognition site of Reelin protein, and not containing an F-spondin domain or a repeat site, wherein the polypeptide is derived from a mouse Reelin polypeptide", "comprising SEQ ID NO:2 and not containing an F-spondin domain or a repeat site," and sequences differing therefrom, all of which are required, "to bind antibody CR-50." Moreover the activity of stimulating the assembly of a Reelin protein molecule, is not limited to mouse Reelin or to anti-Reelin antibody binding activity to which applicants refer within the specification. Neither are the diseases capable of diagnosis and/or treatment referenced by the claim as the specification suggests. The limitations of the specification cannot be read into the claims but must be recited thereby.

In the absence of guidance, a practitioner of the art of molecular biology would have to resort to a substantial amount of experimental trial and error to produce the peptides as claimed. This trial and error would constitute undue experimentation as there is no guidance as to which of the modifications would reasonably correspond to

the structures and/or functions of the claims and therefore, the instant specification is not enabling for the full scope of the peptides claimed. The standard for an enabling disclosure is not one of making and testing and the claims constitute a "wish to know". Because there is no reasonable expectation that any modification would either correspond both structurally and functionally, the experimentation is undue. What is required is some degree of predictability as to those modifications that are appropriate. The instant specification fails to provide the requisite elements and thus one is not provided any expectation of antibody binding.

Applicant has taken the position that 35 U.S.C. § 112, first paragraph, permits an artisan to present claims of essentially limitless breadth so long as the specification provides one with the ability to test any particular embodiment which is encompassed by the material limitations of a claim and thereby distinguish between those embodiments which meet the functional limitations from those embodiments which don't. This argument is not entirely without merit. However, the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. Applicant's 'make and test' position is inconsistent with the decisions in In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) and Amgen v. Chugai Pharmaceuticals Co. Ltd., 13 USPQ2d, 1737 (1990), and In re Wands, 8 USPQ2d, 1400 (CAFC 1988). In re Wands stated that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or

guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of this factors were addressed in the initial rejection. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Clarification of the metes and bounds of the "CR-50 antibody recognition site", "F-spondin domain", "repeat site" and scope of "reelin" peptides as set forth below will further prosecution as to enablement.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10. Claims 4-8 and 10-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Curran et al., US 6,323,177 filed 6-16-1999, issued 11-27-01.

The claims have been interpreted as being drawn to the polynucleotide encoding the polypeptide of withdrawn claim 3. Curran et al., teach Reelin polypeptide sharing 100% similarity with instant SEQ ID NO:2 and polynucleotides encoding the Reelin gene, see in particular 6,323,177, SEQ ID NO:3, residues 970-1320 sharing 100% similarity with instant SEQ ID NO:1, residues 1-351 and encoding SEQ ID NO:2, residues 1-117, see also attached alignment. The '177 patent further teaches isolated nucleic acids inclusive of various insertion, deletion and addition mutants, as well as

fragments thereof encoding particular polypeptides. These mutants include N'- and C'-terminal deletions as recited in column 20, lines 4-14 and column 22, line 48-column 23, line 7. The polypeptides are produced via vector constructs and host cells including fusion proteins as disclosed at columns 9-20 and columns 19-20 in particular. Thus, the patent recognizes polynucleotides encoding SEQ ID NO:2 as claimed in claim 4, polynucleotides of SEQ ID NO:1, as in claim 5, expression vectors, host cells and methods of producing the polypeptide as in claims 6-8. The patent discloses compositions comprising such polynucleotides for stimulating assembly or production of Reelin protein via recombinant DNA technology as in claim 10 and further include such for use in pharmaceutical interventions for example as an antisense nucleic acid treatment, disclosed in column 14, lines 14-30, for viral vector therapy, column 15-17 and for methods of treatment, column 24, lines 14-41, for neuronal migration defects, including those that result in cortical displasia and epilepsy. Thus, the reference teachings anticipate the claimed invention.

Applicants argue in the response of 4-14-03 that because the Curran reference does not teach each and every limitation of the invention, it is not anticipatory. Applicants argue that the reference does not teach the negative limitation of not containing an F-spondin domain or a repeat site.

Applicants arguments filed 4-14-03 have been fully considered but are not persuasive. The prior art reference need not use the same terminology or words to be anticipatory or to describe the same invention. The Curran reference teaches various peptide modifications as disclosed including regions that are N' and C' terminal

truncations and which represent epitope structures of the CR-50 antibody. While applicant's claims do not delimit the residues which correspond to the invention the art and specification clearly establish that the F-spondin domain is within the N'terminus and the repeat region is within the C'terminus. Because the Curran reference teaches such deletions the peptides are within the scope of the claims. Moreover the Curran references such peptides as capable of binding the CR-50 antibody. Thus, the reference teachings anticipate the claimed invention.

New Rejections Necessitated by Amendment

Claim Objections

11. Claim 5 is objected to because of the following informalities: line 4 contains "that of binds" which is nonsensical. Appropriate correction is required.

Claim Rejections - 35 USC § 112

12. Claims 4-8 and 10-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant's claims are amended as indicated in the marked up copy of the amendment submitted 4-14-03. Applicant's point to support for such amendments in claims 4-5, at p. 12, lines 13-19 and at p. 4, lines 19-21. However, the specification and claims fail to support the new recitations. In particular, the peptides appear to optionally include a F-spondin domain or a repeat site as indicated by the or (alternative language)

which differs from the previous negative limitations of not (neither) a F-spondin domain nor a repeat site. Thus, the recitations constitute new matter absent evidence for their support in the specification as originally filed. Moreover, the claims appear to newly recite the element of CR-50 antibody binding. While such limitation is noted with respect to previous claim 5, the recitation is not particularly noted for the peptides as newly claimed that includes either a F-spondin domain or a repeat site. Special attention should be noted to the combination of elements and their full scope.

13. Claims 4-8 and 10-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. With respect to the amended claims requiring antibody CR-50 eptiope structure and binding, the specification is non-enabling because there is insufficient assurance that the antibody is publicly available. While the antibody is recognized in the prior art, the antibody is required to make and use the invention.

The specification lacks deposit information for the deposit of antibody CR-50. Because it is not clear that the antibody is definitively known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the claims require the use of CR-50, a suitable deposit for patent purposes is required. Accordingly, filing of evidence of the public availability of the CR-50 antibody designated as a limitation within claims 4-8 and 10-11 is required. Without publicly available deposit of the above antibody, one of ordinary skill in the art could not be assured of the

ability to practice the invention as claimed. Exact replication of the antibody is an unpredictable event.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of the patent on this application. These requirements are necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required.

If the deposits are not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR § 1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;
3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;

6) The procedures used to obtain a sample if the test is not done by the depository; and

7) A statement that the deposit is capable of reproduction.

As a means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the antibody described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR § 1.801-1.809 for further information concerning deposit practice.

14. Claims 4-8 and 10-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification describes a polypeptide sequence consisting of SEQ ID NO:2. However, the claims as written include polypeptides comprising CR-50 antibody recognition sites of Reelin protein and either a F-spondin domain or a repeat site, but not both. Additionally the claims recite compositions binding antibody CR-50 and that stimulate the assembly of Reelin molecules. However, the instant disclosure of a single polypeptide, that of SEQ ID NO:2, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v*

Eli Lilly & Co, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO: 2 and no other amino acid sequences that are proposed to correspond to the same structural and/or

functional characteristics. Given the fact that the specification fails to provide objective evidence of any additional sequences that are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 4-8 and 10-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants amended claims newly recite "a CR-50 antibody recognition site of Reelin protein and not containing an F-spondin domain or a repeat site," peptides capable of "CR-50 antiboy binding" and compositions stimulating the assembly of "Reelin" protein molecules. While the art, see in particular D'Acrcangelo et al., J. Neurosci., 17:23-31, 1997 (IDS) and de Bergeyck et al., J. of Neurosci. Methods, 82:17-24, 1998 generally teaches such regions and proteins, the references fail to teach the exact residues that correspond to the regions. Thus, applicant's inexact reference to the residues or regions encompassed or excluded by recitations and traversal of the relevant prior art, fails to establish the requisite metes and bounds of the terms within the claim. It is noted that the referrals within the specification at pp. 5 are not exact or definitively defined. Further it is noted that the terminology not...or is indefinite as to whether one or both of the elements is to be absent.

17. Claims 4-8 and 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by de Bergeyck et al., J. of Neurosci. Methods, 82:17-24, 1998.

DeBergeyck et al., teach peptides useful in the generation of various antibodies to the mouse Reeler peptide. In particular, the peptides are represented as in Figure 1B p. 18. Applicant's specification notes that the CR-50 recognition site is within residues 230-346 of Reelin. Peptide H164-496 is noted to be deleted in both the F-spondin region as well as the C'terminal repeat region domains. As the peptide comprises residues 230-346, the CR-50 eptiope region it would bind the CR-50 antibody and the polynucleotides encoding the same residues shares similarity to SEQ ID NO:1. Thus, the peptides anticipate the claimed compositions.

Status of Claims

18. No claims are allowed.

Conclusion

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and

any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

20. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
November 19, 2003

Gary L. Kunz

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600